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EXAMINER

MEHTA, ASHWIN D

ART UNIT	PAPER NUMBER
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1638

16

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/810,764

Applicant(s)

RISTIC ET AL.

Examiner

Ashwin Mehta

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 9-13 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 14-18 and 20-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 March 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-8, 14-18, and 20-31 in Paper No. 15, submitted 21 April 2003 is acknowledged. The traversal is on the ground(s) that the method of claim 19 uses the sequence disclosed as SEQ ID NO: 5 which is specifically claimed in claim 2, and believe that no separate search is required for the non-elected groups as all claims are related as product and method of use. This is not found persuasive because the Examiner maintains that the method of Group III does not require the production of transgenic plants. The method of Group III requires a different analysis from that for the invention of Group I. Further, a search for amino acid sequences would not necessarily reveal information about the genes that encode them.

The requirement is still deemed proper and is therefore made FINAL.

Priority

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The oath/declaration of the instant application indicates that benefit is claimed to provisional applications 60.190,175 and 60/203,204. However, the first sentence on the first page of the specification only indicates that

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benefit is claimed to 60/190,175. The statement should be amended to recite 60/203,204 and its filing date if Applicants wish to claim benefit from it.

Specification

3. The specification is objected to for failing to comply with the sequence rules of 37 CFR 1.821-1.825. An amino acid sequence appears in line 9 of the paragraph bridging pages 10-11 that must be referenced by its sequence identifier.

Claim Objections

4. Claims 20 and 21 are objected to under 37 CFR 1.75 (b) as being duplicate claims. Both claims encompass a transgenic plant containing a DNA construct encoding EF-Tu, wherein expression of EF-Tu expression increases tolerance to heat and/or drought, in comparison to a corresponding untransformed plant. Claim 20 recites that the plant is "substantially tolerant or resistant," whereas claim 21 recites that the plant exhibits tolerance. However, the difference between "substantially tolerant" and "tolerant" is not apparent. The definition for "substantially tolerant" on page 14 indicates that transgenic or transformed plants of the invention have tolerance. The significance of the term "substantially" is not clear. There also does not appear to be any difference between "transformed" and "transgenic," and the terms "tolerant" and "resistant." Applicants are required to cancel one of the claims, or amend the claim(s).

5. Claim 22 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the

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claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 22 attempts to limit the plant of claim 21 by requiring the DNA construct to comprise a promoter. However, the DNA construct of claim 21 inherently comprises a promoter, since claim 21 indicates that the DNA construct is expressed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-8, 14-18, 20, 23, and 27-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1: the term "expressed primarily" in line 5 renders the claim indefinite. It is not clear what is encompassed by "primarily." For example, can the protein be expressed during other times, or only during heat shock? The metes and bounds of the claim are unclear.

Further in claim 1: the recitation "high homology" in line 7 renders the claim indefinite. It is not clear what differentiates high homology from other levels of homology. It is also not clear what "homology" encompasses.

Further in claim 1: the recitation "chloroplast elongation factor EF-Tu, from E. coli" in lines 7-8 renders the claim indefinite. E. coli do not have chloroplasts.

Further in claim 1: the recitation "high stringency" in line 10 renders the claim indefinite. It is not clear what hybridization conditions are considered to be highly stringent. The definition

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of "stringency" in the paragraph bridging pages 14-15 does not define the conditions that are highly stringent.

Further in claim 1: the recitation "(putative coding region)" in lines 10-11 renders the claim indefinite. It is not clear what the meaning of this recitation is in the context of the claimed invention. What it adds to the claimed invention is unclear. The metes and bounds of the claim are unclear.

Further in claim 1: it is not clear if the protein encoded by the nucleotide sequence is approximately 45 kD before, or after, import into the chloroplast, if the nucleotide sequence is from a nuclear gene.

Further in claim 1: the claim indicates that the protein is expressed primarily under heat shock conditions. It is not clear whether this means that the isolated nucleotide sequence also comprises a heat inducible promoter.

In claim 2: the claim limits the nucleotide sequence of claim 1 to be SEQ ID NO: 5. However, SEQ ID NO: 5 sets forth an amino acid sequence.

In claim 3: the recitation "capable of directing expression of a protein" in lines 3-4 renders the claim indefinite. The recitation does not make clear if expression actually occurs, or when or under what conditions. It is suggested that the recitation be replaced with --that directs expression--.

In claim 14: the claim is indefinite because the last recited step is inconsistent with the preamble. Line 1 indicates that the claim is directed to a method for increasing plant tolerance to heat and drought. However, the last recited step results in a transformed plant cell, not a plant. It is suggested that the claim be amended to indicate that the cells comprising the genetic

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construct are regenerated to transgenic plants, wherein expression of said protein increases heat and drought tolerance.

In claim 15: the claim recites the limitation "said expression cassette." There is insufficient antecedent basis for this term in the claim or claim 14.

In claim 17: the claim appears to be missing a step. Claim 17 limits claim 14 by requiring the selection of transgenic plants. However, as discussed above, the last recited step in claim 14 results in transformed cells, not plants. Note that if claim 14 is amended as suggested above, then claim 17 would not be further limiting, since the selection of transgenic plants would be inherent to the method of claim 14.

In claims 20 and 28: the term "substantially" in line 1 of claim 20 and line 8 of claim 28 renders the claims indefinite. It is not clear what is meant by the recitation. As discussed above, the definition for "substantially tolerant" on page 14 indicates that transgenic or transformed plants of the invention have tolerance to heat and/or drought conditions. It is not clear what the significance of the term 'substantially' is in this definition.

In claims 23 and 29: the claims are indefinite because they do not clearly indicate whether the seeds or progeny comprise the DNA construct.

In claim 27: the term "obtainable" in line 2 renders the claim indefinite. It is not clear whether or not the plant is obtained, or what other way the plant is obtained. It is suggested that the term be replaced with --obtained--.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 3-8, 14-18, and 20-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards any purified and isolated nucleotide sequence which encodes a regulatory protein characterized by the following: (a) is approximately 45 kD; (b) is expressed primarily under heat shock conditions; (c) is localized in chloroplasts; (d) has high homology to chloroplast elongation factor EF-Tu, from E. coli or tobacco; said nucleotide sequence being capable of hybridizing under high stringency to SEQ ID NO: 6; any prokaryotic or eukaryotic host cell transformed with a vector comprising an expression construct comprising said nucleotide sequence; a method for increasing plant tolerance to heat and drought, comprising introducing to a plant cell a genetic construct comprising said nucleotide sequence; a transformed plant containing a DNA construct encoding EF-Tu, wherein expression of EF-Tu confers tolerance to heat and/or drought; seed or progeny produced from said transgenic plant.

The specification indicates that a maize line, designated "ZPBL 1304" (1304), showed increased heat stability of chloroplasts versus those of other maize lines. When ZPBL 1304 was exposed to stress conditions comprising a 7-day soil drying and 6h at 45°C, chloroplasts structure was similar to that under non-stress conditions. In a stress sensitive line, ZPL 389 (389), chloroplasts structure was damaged (pages 34-35). Under a more severe stress treatment,

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1304 chloroplasts showed varying degrees of damage, but recovered several days after the plant was rewatered. Chloroplasts from 389, however, did not recover under the same conditions (pages 35-36). The specification indicates that a unique band of 45 kD heat shock proteins was found in heated 1304 plants but not heated 389 plants (page 38). Two-dimensional gel electrophoresis of proteins extracted from heated 1304 leaves showed the presence of 5 proteins. The individual spots were removed and subjected to N-terminal protein sequencing (Example 3). The N-terminal sequences of polypeptides 2, 4, and 5, had similarity to protein elongation factor Ef-Tu of prokaryotes, lower eukaryotes, and chloroplast of higher plants. The sequence (20 amino acids) from polypeptide 2 showed, 80% similarity to chloroplast Ef-Tu of plants including that of *Arabidopsis thaliana*. The sequence from polypeptides 4 and 5 showed 80 to 90% similarity to Ef-Tu. Polypeptide 3 showed more than 80% homology to glyceraldehydes 3-phosphate dehydrogenase (page 44). Reproducible sequence was not obtained from polypeptide 1. Subcellular localization analysis showed that polypeptides 1-3 and 5 localized to chloroplasts, whereas polypeptide 4 was in the cytosol (page 45). Analysis of proteins synthesized by isolated chloroplasts revealed that these 45 kD proteins were not synthesized in chloroplasts (page 46). A maize EST database was searched with the peptide sequences, and matched various EF-Tu genes. One clone was selected which had high homology with a tobacco chloroplast elongation factor. The specification indicates that a cDNA that appeared to be full length was isolated from a cDNA library constructed from the maize line, B73. The cDNA sequence is in SEQ ID NO: 6 (page 50). Maize EF-Tu cDNA was overexpressed in *Escherichia coli*. The number of *E. coli* colonies that grew at 37°C following heat stress was greater cells induced to express the maize cDNA versus those that were not (pages 50-51).

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However, the specification does not describe any other nucleotide sequence encoding a 45 kD chloroplast protein expressed primarily during heat shock, and having high homology to chloroplast EF-Tu from E. coli or tobacco, or further capable of hybridizing under high stringency conditions to SEQ ID NO: 6, other than SEQ ID NO: 6. The specification does not teach how the sequence of SEQ ID NO: 6 may differ without altering its functional activity. As the specification does not define "high homology" and "high stringency", and therefore the specification does not describe the structural relationship of the claimed nucleotide sequences to SEQ ID NO: 6. Further, the claims encompass EF-Tu proteins that do not have the activity of conferring heat and drought tolerance to transgenic plants: claim 1 does not indicate that the regulatory protein has any activity other than that of an elongation factor. See Fiers 25 USPQ 2d (CAFC 1993) at 1606, which states that "[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". Given the breadth of the claims and lack of guidance as discussed above, the specification fails to provide an adequate written description of the multitude of nucleotide sequences encompassed by the claims.

8. Claims 1, 3-8, 14-18, and 20-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn towards any purified and isolated nucleotide sequence which encodes a regulatory protein characterized by the following: (a) is approximately 45 kD;

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(b) is expressed primarily under heat shock conditions; (c) is localized in chloroplasts; (d) has high homology to chloroplast elongation factor EF-Tu, from *E. coli* or tobacco; said nucleotide sequence being capable of hybridizing under high stringency to SEQ ID NO: 6; any prokaryotic or eukaryotic host cell transformed with a vector comprising an expression construct comprising said nucleotide sequence; a method for increasing plant tolerance to heat and drought, comprising introducing to a plant cell a genetic construct comprising said nucleotide sequence; a transformed plant containing a DNA construct encoding EF-Tu, wherein expression of EF-Tu confers tolerance to heat and/or drought; seed or progeny produced from said transgenic plant.

The specification indicates that a maize line, designated "ZPBL 1304" (1304), showed increased heat stability of chloroplasts versus those of other maize lines. When ZPBL 1304 was exposed to stress conditions comprising a 7-day soil drying and 6h at 45°C, chloroplasts structure was similar to that under non-stress conditions. In a stress sensitive line, ZPL 389 (389), chloroplasts structure was damaged (pages 34-35). Under a more severe stress treatment, 1304 chloroplasts showed varying degrees of damage, but recovered several days after the plant was rewatered. Chloroplasts from 389, however, did not recover under the same conditions (pages 35-36). The specification indicates that a unique band of 45 kD heat shock proteins was found in heated 1304 plants but not heated 389 plants (page 38). Two-dimensional gel electrophoresis of proteins extracted from heated 1304 leaves showed the presence of 5 proteins. The individual spots were removed and subjected to N-terminal protein sequencing (Example 3). The N-terminal sequences of polypeptides 2, 4, and 5, had similarity to protein elongation factor Ef-Tu of prokaryotes, lower eukaryotes, and chloroplast of higher plants. The sequence (20 amino acids) from polypeptide 2 showed, 80% similarity to chloroplast Ef-Tu of plants including

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However, the specification does not teach other isolated nucleotide sequences encoding a 45 kD chloroplast protein expressed primarily during heat shock, and having high homology to chloroplast EF-Tu from *E. coli* or tobacco, or further capable of hybridizing under high stringency conditions to SEQ ID NO: 6, other than SEQ ID NO: 6. The specification indicates the presence of multiple 45 kD proteins, that may be EF-Tu proteins, in the chloroplasts of maize plant ZPBL 1304 under heat shock conditions. However, the nucleotide sequences encoding these proteins have not been reduced to practice. See In re Bell, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and In re Deuel, 34 USPQ2d, 1210 (Fed. Cir. 1995), which teach that the mere existence of a protein does not enable claims drawn to a nucleic acid encoding that protein. See

also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence), and at page 1027, where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Further, the specification does not teach that plants transformed with any nucleotide sequence encoding a chloroplast EF-Tu was produced, wherein expression of the EF-Tu conferred increased resistance to drought and/or heat to the plant. It is unpredictable that the transgenic expression of the claimed nucleotide sequence in transgenic plants would confer increased drought and/or heat resistance. SEQ ID NO: 6 is not the only coding sequence that is expressed in 1304 chloroplasts under stress conditions, and this is assuming that SEQ ID NO: 6 actually encodes one of the 45 kD proteins. The specification does not confirm that SEQ ID NO: 6 actually does encode one of the proteins. The specification shows that the expression of several proteins were increased in 1304 chloroplasts under heat and drought conditions, not all of which encode EF-Tu. The specification admits that one of these proteins showed more than 80% homology to glyceraldehyde 3-phosphate dehydrogenase (page 44). Further, the claim invention encompasses expressing any EF-Tu in transgenic plants, including those that are not localized to the chloroplast or whose expression is not increased during heat or drought conditions. The specification does not teach that any such EF-Tu proteins are involved in conferring heat or drought resistance. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

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Furthermore, claim 7 encompasses non-plant host cells transformed with the claimed isolated nucleotide sequence. As the specification teaches that the exemplified EF-Tu of the invention is expressed in chloroplast, it is not clear what function it would have in other eukaryotic cells. Such non-plant host cells would already have endogenous elongation factors, and as they do not have chloroplasts, it is not clear, and not taught in the specification, how one would use them. See Genentech, Inc. V. Novo Nordisk, A/S, supra. It is suggested that claim 7 be amended to encompass only bacterial and plant host cells. Given the breadth of the claims, unpredictability of the art and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless —

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Murayama et al. (Plant Mol. Biol, 1993, Vol. 22, pages 767-774).

The claim is broadly drawn towards any purified and isolated nucleotide sequence which encodes a regulatory protein characterized by the following: (a) is approximately 45 kD; (b) is expressed primarily under heat shock conditions; (c) is localized in chloroplasts; (d) has high

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homology to chloroplast elongation factor EF-Tu, from E. coli or tobacco; said nucleotide sequence being capable of hybridizing under high stringency to SEQ ID NO: 6;


Murayama et al. teach a cDNA sequence encoding a 45 kD tobacco chloroplast EF-Tu (pages 770-771). The properties of being expressed primarily under heat shock conditions, and hybridizing under high stringency conditions, are inherent to the protein, absent evidence to the contrary.

10. No claim is allowed.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

June 25, 2003


ASHWIN D. MEHTA, PH.D
PATENT EXAMINER